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LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,433	BROLIDEN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sh et with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46,57-61 and 72-74* is/are rejected.

7)☒ Claim(s) *47-56 and 62-71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 44-74 are currently pending and under consideration in the application. Claims 1-8, 18-25, and 34-43 were under consideration and rejected in the prior action, mailed on

2. Because new rejections have been raised in this action that were not made of issue in the prior action, or necessitated by amendment to the claims, this action is being made Non-Final.

Election/Restrictions

3. Applicant's election without traverse of Group I, and of subgroup (a)(wherein the capsid agent comprises the sequence glutamine-glutamine-tyrosine, hereinafter QQY), and species (1) in Paper No. 9 is acknowledged.

4. Claims 9-17, and 26-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Information Disclosure Statement

5. It is noted that copy provided of reference 21 of the IDS filed on August 27, 2002, includes only pages 1 and 2 of the reference, the introduction. The reference has been considered only the extent of the material contained in that portion of the reference provided.

6. Reference 19 of the IDS filed on August 27, 2002 is identified as a PCT publication with an English abstract. As the reference is in a foreign language, and no other translation of the reference has been provided, the reference has been considered only to the extent of the contents of the abstract in the English language.

Drawings

7. New corrected drawings are required in this application for the reasons indicated on the attached Form PTO 948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Priority

8. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) (the Swedish parent Application 9804022-3) which papers have been placed of record in the file.

Specification

9. **(Prior Objection- Withdrawn)** The disclosure was objected to because of the following informalities: On page 25-27, the disclosure refers to Figures A-H, each showing a graph of cell growth inhibition by different pools of VP2 peptides. The various pools in the figures are referred to as pools I-VIII. However, in identifying the peptides on pages 26 to 27, the

specification refers to pools 1-8. As indicated in the prior action, it was assumed that pool I of figure 8A comprises the peptides of pool 1 of page 26, with the remaining pools matched accordingly. Clarification of such by using the same numeric identification was requested. In view of the amendments to the description of Figure 8, the objection is withdrawn.

10. **(New Objection)** The drawing of Figure 9 is objected to for the reasons indicated with respect to Figure 8 in the prior action. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

11. **(New Objection)** Claims 45 and 60 are objected to because of the following informalities: the claims are objected to for the phrase "comprises VP1 and VP2 protein." The claims may be more correctly amended to read on methods wherein the capsid agent --comprises the VP1 and VP2 proteins.-- Appropriate correction is required.

12. **(New Objection)** Claims 46 and 61 are objected to because of the following informalities: the claims are objected to for the phrase "comprises VP2 protein." The claims may be more correctly amended to read on methods wherein the capsid agent --comprises the VP2 protein. -- Appropriate correction is required.

13. **(New Objection)** Claims 57 and 58 are objected to because of the following informalities: the claims are objected to for the phrase "comprises VP1 protein," or "comprises of VP2 protein." The claims may be more correctly amended to read on methods wherein the capsid agent --comprises the-- identified protein. Appropriate correction is required.

14. **(New Objection)** Applicant is advised that should claim 46 be found allowable, claim 58 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. **(Prior Rejections- Withdrawn)** Claims 1-8, 18-25, and 34-43 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims were rejected on various grounds. In view of the cancellation of these claims, and the corrected language of new claims 44-74, all of the previous indefiniteness rejections are withdrawn.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. **(Prior Rejection- Maintained)** Claims 1, 2, 4, 7, 8, 18, 19, 21, 24, and 25 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The identified claims have been cancelled, and new claim 74, which reads on the rejected subject matter, has been adder to the application. In view of the limitation of new claims 44-73 to B`9 capsid agents comprising the trimer QQY, the rejection is not extended to these claims. However, claim 74 reads on any fragment of the VP2 protein that is of sufficient length to inhibit hematopoiesis. Thus, while the rejection is rendered moot with respect to the previously rejected (and now cancelled) claims, the rejection hereby extended to new claim 74.

In traversal of the rejection as applied against the previously rejected claims, the Applicant argues that the Examiner has misapplied the Written Description requirement. The Applicant argues that they are not required to "describe exactly the subject matter claimed," and that the examples that they have provided are sufficient. The Examiner agrees that the Applicant need not provide a description of every possible fragment of the VP2 protein with the claimed function in order to satisfy the written description requirement. However, while the Applicant has provided examples of peptides of several lengths that are capable of inhibiting hematopoiesis, all of the peptides that are specifically disclosed as having this function are among those that comprise the QQY trimer (Table 7). While the Applicant has also disclosed

pools of several different (overlapping) peptides that apparently have the claimed function (Table 6), the Applicant has not identified the specific sequence (or sequences) within those pools, other than those with the QQY trimer, that are responsible for the pools being able to induce the desired response. Thus, the Applicant has provided only three known structures that have been demonstrated to have a correlation to inhibition of hematopoiesis: the complete VP1 and VP2 proteins, and fragments of the VP2 protein comprising the QQY trimer.

The Examiner agrees with the Applicant that the Federal Circuit's decisions in Eli Lilly, and Moba state that a functional requirement need not necessarily fail as providing sufficient written description for a genus of genetic material. However, in both the excerpts from Eli Lilly (prior action) and from Moba (Response), the court continues its discussion to clarify the decisions by "the requirement may be satisfied if in the knowledge in the art the disclosed function is sufficiently correlated to a *particular, known structure*" (emphasis added). Moba, 44 U.S.P.Q. 2d at 1438-39 (citing Amgen, 314 F.3d at 1332), As has been described above, the Applicant has not correlated any "particular" structure, other than the QQY trimer, in the VP2 protein that may be correlated to the identified function. While the Applicant has provided groups of fragments that contain some structure providing the function, there is no particular structure in these pools that has been shown to correlate to the function. Thus, while the Applicant has provided support for fragments comprising the QQY trimer, the Applicant has not provided sufficient written description to support claims to *any* fragment of the VP2 protein that can inhibit hematopoiesis.

It is noted that the claims have been amended such that they now read on fragments of sufficient length to inhibit hematopoiesis. However, as the Applicant has not shown a correlation

between the claimed function and any structure other than the QQY trimer, the Applicant has not provided adequate description of what a sufficient length to inhibit hematopoiesis would comprise. While a trimer comprising the QQY sequence may be sufficient, it is not known what lengths of fragments not comprising the QQY sequence would also be of sufficient length. Thus, there is insufficient written description for the fragments of new claim 74 for substantially the same reasons as indicated above and in the prior action with regards claims reading on any fragment of at least 3 residues. The rejection is therefore extended to, and maintained over new claim 74.

19. **(Prior Rejection- Maintained)** Claims 1-8, 18-25, and 34-43 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting the growth of hematopoietic cells by administering to a subject a B19 parvovirus VP2 capsid, or certain fragments thereof, does not reasonably provide enablement for using any fragment of the VP2 capsid to treat a subject for any hematopoietic disorder. The above claims have been cancelled, and replaced by new claims 44-74. The rejection is not extended to claims 44-73. However, new claim 74 reads on methods of inhibiting hematopoiesis through the administration of a VP2 fragment "of sufficient length to inhibit hematopoiesis." This claim is broader then the previously rejected claims in that it does not require a minimum length for the fragments.

The rejection is maintained against new claim 74. The Applicant has shown that there may be other fragments, from those comprising the QQY sequence, from the VP2 protein that perform the clamed function. As argued by the Applicant, and supported by the Declaration of

Anders Vahlne, the Applicants have demonstrated that pools comprising other fragments of the protein were effective at inhibiting hematopoiesis to some extent. However, the Applicant has not provided sufficient information such that those in the art would know what minimal structures are required to perform the claimed methods. The Applicant has identified only one apparently minimal fragment as per the claimed methods- the QQY fragment. This fragment is present in only one of the various pools of peptide fragments, and therefore does not provide much, if any, guidance that would aid in the identification of other such peptides. It is not known, from any of the other pools, what sequence or combination of sequences, enabled the pools to work. There is no common structure among the different pools by which one skilled in the art could make a prediction as to what such sequences may be. Because those in the art have been taught what sequence or combination of sequence from each pools are necessary to perform the claimed methods, they have also not been taught what a "length sufficient to inhibit hematopoiesis" would comprise.

Thus, in claiming any fragment of sufficient size to perform the claimed function, the Applicant has left it up to those in the art to discover for themselves what other sequences (or combinations of sequences) are necessary to perform the claimed function. Thus, for each of the pools, those in the art must both identify the peptide(s) required to practice the claimed method, and the minimal structure from these peptides that is capable of doing so. They are provided little guidance other than the results from the pools as a whole, and have no means by which to predict the structure of the sequences, or the length of the sequences, required to perform the claimed methods. Thus, while the Examiner agrees with the Applicant and the Declarant that the Applicant has shown that there are other structures within the VP2 protein that may inhibit

hematopoiesis, the Applicant has not provided sufficient information to enable those in the art to identify and use such fragments in the presently claimed methods. In view of this, the enablement rejection of the previously cancelled claims is extended to, and maintained against, pending claim 74.

20. **(New Rejection)** Claims 44-46, 57-61, and 72-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The application does not provide adequate description for any capsid agent, including any VP1 or VP2 proteins, that may inhibit hematopoiesis. The claims have been described above, except that they have been described above and in the prior actions as reading on only capsid agents from the B19 parvovirus. However, the claims actually read on methods of using any capsid agent, either comprising the QQY sequence, or comprising a VP2 fragment of sufficient length to inhibit hematopoiesis.

While the claims broadly read on the use of any capsid agent, the specification clearly indicates in numerous instances that the only capsid proteins that have been conceived of by the Applicant are those comprising the VP1 or VP2 proteins (or fragments of the VP2 protein) from the B19 parvovirus. See e.g., pages 1, lines 12-18; and page 5, lines 8-15. Nowhere does the Applicant suggest that VP2 proteins or capsid particles of other viruses may be used in the claimed methods. Thus, the Applicant has not provided adequate written description for the full scope of the claimed inventions.

21. **(New Rejection)** Claims 44-46, 57-61, and 72-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting hematopoiesis with certain B19 parvovirus capsid agents, does not reasonably provide enablement for methods of using any capsid agents, or any capsid agent comprising the sequence QQY. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims have been described above.

Also as indicated above, the specification does not provide any guidance or suggestion as to any capsid agents, other than those from the B19 parvovirus, that may be used in the claimed methods. While the art is replete with viral capsids, including both Vp1 and Vp2 proteins (see e.g. abstracts of Gharakhanian et al., J Gen Virol 84: 2111-2116; and Jean et al., App Environ Microbiol 67: 5593-5600), there is no suggestion in either the current specification or the art in general that all such proteins would be effective for the inhibition of hematopoiesis. Nor is there any guidance as to what other viral capsids would comprise a protein with a QQY sequence.

Further, even if those in the art could be expected to know what other capsids comprise a QQY sequence, it is not known that all such capsid agents would be operative in the claimed methods. In support of this, it is known both that the effects of substitutions on proteins are unpredictable, and that those in the art are not able to routinely and correctly identify the functions of all proteins from homology alone. See, Bowie et al., Science 247: 1306-10 (teaching that while many protein residues are open to substitution, some substitutions may effect function directly, or affect function by changing the protein structure); and Bork et al., Genome Res 10:

398-400 (teaching that those in the art are able to predict the functions of whole proteins with a accuracy of only 70%). Thus, once other capsids comprising a QQY sequence had been identified, those in the art would still not know if the agents had the necessary function. The ability of the sequence to inhibit hematopoiesis in such other capsid may be hindered due to differences in the position of the sequence in the protein, and the overall structure of the protein.

Thus, the claims read on methods of using a large genus of potential capsid agents. However, there is little guidance to those in the art in the identification of other potentially operative agents, and an absence of working examples from any virus other than the B19 parvovirus. In combination with the broad potential scope, and the lack of guidance, those in the art would have to conduct numerous experiments in a complex and unpredictable art. In view of this, the Applicant has not provided an enabling disclosure for the use of any capsid agent, or any capsid agent comprising the QQY sequence, for the inhibition of hematopoiesis. It is suggested that the claims be amended to read on methods using a capsid agent from the B19 parvovirus.

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 45, 46, 58, 60, 61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-24, 28, 29, 32-34 of copending Application No. 10/200,616. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims merely use alternative language to claim the same methods.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

24. Claims 47-56, and 62-71 are objected to a depending from rejected claims.

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
October 30, 2003

JAMES HOUSEL 11/3/03
SUPERVISORY PATENT EXAMINER
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